June 16, 2005

Elmer Rauckman, Ph.D., DABT
Consulting Toxicologist
BASF Corporation
1201 Anise Court
Freeburg, IL 62243

Dear Dr. Rauckman:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Alkenes, C6-10, Hydroformylation Products, High-Boiling posted on the ChemRTK HPV Challenge Program Web site on February 27, 2004. I commend BASF Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that BASF Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: M. E. Weber
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
High-Boiling Hydroformylation Products of C6-C10 Alkenes

Summary of EPA Comments

The sponsor, BASF Corporation, submitted a test plan and robust summaries to EPA for the high-boiling products of the hydroformylation of C6-C10 alkenes (also known collectively as EP-290) dated December 30, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on February 27, 2004.

EPA has reviewed this submission and reached the following conclusions:

1. Physicochemical Properties. The water solubility data, estimated for various components, are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data on a representative chemical, such as C17 alcohol.

2. Environmental Fate. The biodegradation data are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide data representative of higher molecular weight alkenes and alcohols.

3. Health Effects. The data are adequate for the purposes of the HPV Challenge Program. The reproductive toxicity data from the repeated-dose study need to be available as a separate robust summary. The submitter needs to address deficiencies in robust summaries.

4. Ecological Effects. The acute toxicity data for invertebrates are adequate for the purposes of the HPV Challenge Program. Acute toxicity data for fish and algae and chronic data for invertebrates are needed to satisfy these endpoints.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the High-boiling Hydroformylation Products
Of C6-c10 Alkenes Challenge Submission

Test Plan

General. EP-290 is a mixture of alcohols, acetals, alkenes, ethers, esters, and carboxylic acids. The main component class is aliphatic alcohols, which can comprise up to about 70% of the mixture. Higher molecular weight alkenes, the next largest component class, can comprise up to 25% of the mixture. The carboxylic acids present (4-5%) will behave like naturally occurring fatty acids. The remaining nonalcohol components have log Kow values between 8 and 11.5; these highly lipophilic materials are not expected to be absorbed via any route of exposure.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for all endpoints except water solubility are adequate for the purposes of the HPV Challenge Program.

Water solubility. The submitter needs to provide measured water solubility for representative chemicals instead of estimated data for various components to satisfy this endpoint. According to the test plan, C13–C20 alcohols comprise the highest percentage (32.0% - 38.0%) of a typical mixture. The submitter needs to provide measured water solubility data for one of these alcohols, such as C17; a measured water solubility is also recommended for one of the higher molecular weight alkenes, which can comprise up to 25% of an EP-290 commercial mixture.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for all endpoints except biodegradation are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitter needs to provide data on representative higher molecular weight alkenes and alcohols. Given the lower expected water solubility of these chemicals, there is no assurance that they will degrade at rates comparable to the lower molecular weight components for which data were provided. Up to 25% of EP-290 consists of higher molecular weight alkenes, with a typical composition being 5.5%–7.5% hexadecene, 9%–11% octadecene, and 5%–7% eicosene. The only data provided are for C9–C11 (C10 rich) alkenes, which may not be representative. The submitter needs to provide biodegradation data, following OECD TG 301, for hexadecene, octadecene, or eicosene.

Similarly, for the aliphatic alcohols, a typical composition includes 32%–38% C13-C20 alcohols and 10%–12% >C21 alcohols. The only data provided are for olefin hydroformylation products C9–C11 (C10 rich) iso and olefin hydroformylation products C11–C14 (C13 rich) iso. The submitter needs to provide biodegradation data, following OECD TG 301, for one or more higher molecular weight alcohols, preferably ≥C20.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Data on EP-290 itself were provided for acute and repeated-dose toxicity. For genetic, reproductive, and developmental toxicity, the submitter provided data on individual components, component mixtures or related chemicals. The data are adequate for the purposes of the HPV Challenge Program.

Repeated-Dose Toxicity. The subheading indicated that the study was by the oral route, whereas it was an aerosol inhalation study. The submitter needs to make the appropriate corrections to the test plan.

Genetic toxicity. For mutagenicity and chromosomal aberrations, data were submitted for individual components: behenyl alcohol (C-22), alkenes (branched and linear), 1-octadecene and the related chemicals 2-ethylhexanol (C-8) and 1-tetradecene. The genetic toxicity endpoint has been adequately characterized by the submitted data. No robust summaries were provided for 2-ethylhexanol; however, those summaries are available in another BASF submission, 2-Ethylhexanol Heavies, posted on the Chem RTK website on February 4, 2005. The submitter should reference the latter submission.

Reproductive toxicity. A combined screening study (a modified OECD TG 422) of 1-tetradecene and a one-generation reproduction study of 1-docosanol were submitted for this endpoint. Also, the repeated-dose study of EP-290 included histopathologic examination of the reproductive organs. While tetradecene does not directly represent EP-290, it lies just below the low end of the EP-290 olefin range and provides a conservative estimate of toxicity for the olefinic components. This is because, as is generally accepted, the lower homologue is expected to be more water-soluble and absorbable, and thus more likely to elicit mammalian toxicity, than its longer chain homologues (as confirmed by the lack of effects observed with 1-docosanol). In this case, therefore, EPA believes that the reproductive toxicity endpoint can be adequately characterized using the available reproductive/ developmental data for EP-290, 1-tetradecene and 1-docosanol.

Developmental toxicity. Data were submitted for a mixture of C7-11 linear and alpha-methyl branched alcohols. 1-Tetradecene (CAS # 1120-36-1) is also used in a modified OECD TG 422 to cover this endpoint. While these chemicals are not directly representative of the submitter's HPV chemical mixture, both lie just below the low end of the ranges of the corresponding EP-290 constituents, i.e., alcohols and olefins, respectively, and provide conservative estimates of toxicity for those components as discussed above under "Reproductive toxicity". EPA believes that the developmental toxicity endpoint can be adequately characterized in this case using the available reproductive/developmental data for "C7-11 linear and alpha-methyl branched alcohols" and 1-tetradecene.

Ecotoxicity (fish, invertebrates, and algae)

Fish, Invertebrates, and Algae. The acute test data for invertebrates are adequate for the purposes of the HPV Challenge Program, but acute data for algae and fish are inadequate. There are no data for algae, and the fish studies were conducted above the water solubility limit. In addition, a chronic daphnid test (21-day reproduction) is indicated by the high log Kow values of most of the EP-290 constituents. While a chronic daphnid test generally obviates the need for further acute testing, the significant acute toxicity observed in invertebrates underlines the need for a complete acute test battery in the case of this complex mixture. Therefore, acute fish and algae tests are needed using the OECD's "Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures" [http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/env-jm-mono(2000)6].

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The summary for the acute inhalation study should state whether exposures were whole-body or nose only. The clinical observations should be tabulated to include exposure concentration, time of observation, and animal response to exposure. The summary for the acute dermal study should include a description of test area conditions and any scoring or grading method used. OECD TG 402 recommends 5 animals/dose or 5/sex if the limit dose is used. The statement "Procedure is similar to current OECD-423 Acute Toxic Class Method" should be deleted, as this method refers to acute oral testing. The submitter needs to report whether or not body weight determinations were made and tabulate toxicity findings by dose level and sex.

Repeated-Dose Toxicity. The summary should state whether exposures were whole-body or nose only. Any statistical methods used to analyze the data should also be identified.

Genetic Toxicity. The data need to be tabulated to show the mean number of revertants per plate and standard deviations for each chemical.

Reproductive Toxicity. A robust summary outlining the histopathologic evaluation of the reproductive organs from the repeated-dose toxicity study with EP-290 needs to be prepared.

Ecological Effects

Invertebrates. The summary of the acute study in *Daphnia magna* should include adequate details about the composition of substance tested, test guideline/standardized test method used, GLP compliance, age of daphnids used, photoperiod, and results of statistical analyses used.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.